Remarks

Applicants responded to the Office Action mailed January 2, 2002 via facsimile on May 2, 2002. However, in that Response Applicants inadvertently failed to address the issue of the Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Sequence Disclosures. In accordance with 37 C.F.R. §1.821(c) an (e), a Sequence Listing in paper form and a copy of the Sequence Listing in computer readable form are submitted herewith. Applicants believe the current response completes the requirements for the sequence listings set forth in the Office Action.

Applicants respectfully submit that the contents of the paper version of the Sequence Listing and the computer readable version of the Sequence Listing are the same and do not add new matter.

Amendments to the specification are made to insert SEQ ID NOs as appropriate.

Claims 4, 14, 22, 24, 27, and 32 having been amended, the pending claims are claims 4-8 and 14-32. Reconsideration and withdrawal of the rejections are respectfully requested.

The amended claims are fully supported by the originally filed claims and the specification. For example, the sequence in claim 22 is supported by the specification at page 5, lines 29-30. The language regarding the non-peptide moieties in claim 32 is supported by the specification at page 7, lines 22-35 and page 9, line 57. No new matter has been added.

Summary

It is respectfully submitted that the pending claims 4-8 and 14-32 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
FIELDS et al.

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CERTIFICATE UNDER 37 CFR §1.10:
"Express Mail" mailing label number: EV 073732125 US Date of Deposit: June 3, 2002
The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

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APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/529,691
Docket No.: 110.00680101

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been shaded.

In the Specification

The paragraph beginning at page 5, line 16, has been amended as follows:

Figures 1A and 1B show the relative inhibition of M14#5 human melanoma cell adhesion to 10 µg/mL type IV collagen (TIV), fibronectin (FN), laminin (LM), or bovine serum albumin (BSA) by 100 µg/mL of L-IVH1, D-IVH1, or RI-IVH1 (a polypeptide having the sequence pro-ala-gly-pro-trp-gly-pro-asn-gly-lys-asp-gly-lys-val-gly (SEQ ID NO:3), which is the all-D form synthesized in the reverse order and referred to as "Retro-Inverso"). Cells were preincubated with the peptides for 15 minutes and then added to the wells in the presence of the peptides for a 30-minute incubation period at 37°C. The data represent the means of triplicate points plus or minus the standard errors of the means. Figures 1A and 1B represent different experiments run under the same conditions.

The paragraph beginning at page 5, line 27, has been amended as follows:

Figure 2A and B show the inhibition of M14#5 human melanoma cell invasion through MATRIGEL by 500 µg/mL (A) or 1 mg/mL (B) of L-IVH1, D-IVH1, or RI-IVH1 (a polypeptide having the sequence pro-ala-gly-pro-trp-gly-pro-asn-gly-lys-asp-gly-lys-val-gly (SEQ ID NO:3), which is the all-D form synthesized in the reverse order and referred to as "Retro-Inverso"). Cells were mixed with the peptides and then tested for their ability to invade through MATRIGEL basement membrane (obtained from Collaborative Biomedical Products). The data represents the means of triplicate points plus or minus the standard errors of the means.

The paragraph beginning at page 13, line 8, has been amended as follows:

To synthesize either a peptide or peptide-conjugate containing a cytotoxic agent, one would need to assemble the toxin, such as the risin A chain, onto the α-amino group of the peptide and the α- or ε-amino group of the peptide-conjugate. For example, the all-D IV-H1 is synthesized, and the risin A chain sequence (Gln-Tyr-Ile-Lys-Ala-Asn-Ser-Lys-Phe-Ile-Gly-Ile-Thr-Glu) (SEQ ID NO:4) is assembled onto the *N*-terminus of the resin-bound IV-H1 sequence by standard solid-phase methods (G. Fields et al., *Synthetic Peptides: A User's Guide* (Grant, G.A. ed.), pp. 77-183, W.H. Freeman & Co., New York (1992)). A spacer such as 6-aminohexaonic acid may or may not be included between the IV-H1 and risin A sequences. Alternatively, for peptide-conjugates, the all-D IV-H1 is synthesized, an Fmoc-Lys(Dde) residue is incorporated (where Dde is 1-(4,4-dimethyl-2,6-dioxocyclohex-1-ylidene)-ethyl), the Fmoc group is removed, and the risin A chain sequence is added to the resin-bound peptide. The Dde group is removed with hydrazine (C. Fields et al., *Biopolymers*, *33*, 1695-1707 (1993) and the conjugate (alkyl tail or PEG) is added to the *N*-ε-amino group of the resin-bound peptide. The peptide or peptide-conjugate is then purified and characterized as described above.

In the Claims

For convenience, all pending claims are shown below.

4. (Twice Amended) A polypeptide having the sequence gly-val-lys-gly-asp-lys-gly-asn-pro-gly-trp-pro-gly-ala-pro (SEQ ID NO:1), which is in the all D-form.

5. The polypeptide of claim 4 further comprising a cytotoxic agent covalently bonded thereto.

6. The polypeptide of claim 4 which inhibits binding of tumor cells to type IV collagen.

7. The polypeptide of claim 4 which inhibits tumor cell invasion into basement membranes.

8. The polypeptide of claim 4 which inhibits tumor cell metastasis.

14. (Twice Amended) A peptide-conjugate comprising a polypeptide having the sequence gly-val-lys-gly-asp-lys-gly-asn-pro-gly-trp-pro-gly-ala-pro (SEQ ID NO:1), which is in the all D-form, wherein the polypeptide is bonded to a non-peptide moiety.

15. The peptide-conjugate of claim 14 further comprising a cytotoxic agent covalently bonded thereto.

16. A method of inhibiting tumor cell binding to type IV collagen comprising contacting the tumor cell with a polypeptide of claim 4 or a peptide-conjugate of claim 14.

17. A method of inhibiting tumor cell invasion of a basement membrane comprising modulating the tumor cell with a polypeptide of claim 4 or a peptide-conjugate of claim 14.

18. A method of inhibiting tumor cell metastasis comprising modulating the tumor cell with a polypeptide of claim 4 or a peptide-conjugate of claim 14.

19. The method of claim 16 which is carried out *in vivo*.

20. The method of claim 17 which is carried out *in vivo*.

21. The method of claim 18 which is carried out *in vivo*.

22. (Amended) A polypeptide having the sequence pro-ala-gly-pro-trp-gly-pro-asn-gly-lys-

asp-gly-lys-val-gly (SEQ ID NO:3), which is in the all D-form.

23. The polypeptide of claim 22 further comprising a cytotoxic agent covalently bonded thereto.

24. (Amended) [t]The polypeptide of claim 22 which inhibits binding of tumor cells to type IV collagen.

25. The polypeptide of claim 22 which inhibits tumor cell invasion into basement membranes.

26. The polypeptide of claim 22 which inhibits tumor cell metastatis.

27. (Amended) A peptide-conjugate comprising a polypeptide pro-ala-gly-pro-trp-gly-pro-asn-gly-lys-asp-gly-lys-val-gly (SEQ ID NO:3), which is in the all D-form, wherein the polypeptide is bonded to a non-peptide moiety.

28. The peptide-conjugate of claim 27 further comprising a cytotoxic agent covalently bonded thereto.

29. A method of inhibiting tumor cell binding to type IV collagen comprising contacting the tumor cell with a polypeptide of claim 22 or a peptide-conjugate of claim 27.

30. A method of inhibiting tumor cell invasion of a basement membrane comprising modulating the tumor cell with a polypeptide of claim 22 or a peptide-conjugate of claim 27.

31. A method of inhibiting tumor cell metastatis comprising modulating the tumor cell with a

polypeptide of claim 22 or a peptide-conjugate of claim 27.

32. (Amended) A peptide-conjugate comprising a polypeptide having the sequence gly-val-lys-gly-asp-lys-gly-asn-pro-gly-trp-pro-gly-ala-pro (SEQ ID NO:1), which is in the all L-form, wherein the polypeptide is bonded to a non-peptide moiety selected from the group consisting of an organic group having an alkyl chain, a phospholipid, a polyalkylene glycol, a DNA intercalator, a metal chelator, an alkylating agent, and a membrane-disrupting agent.